6/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07181774 93049181 PMID: 1385114
The human T cell antigen gp39, a member of the TNF gene family, is a ligand for the CD40 receptor: expression of a soluble form of gp39 with B cell co-stimulatory activity.
Hollenbaugh D; Grosmaire LS; Kullas CD; Chalupny NJ; Braesch-Andersen S; Noelle RJ; Stamenkovic I; Ledbetter JA; Aruffo A
Bristol-Myers Squibb Pharmaceutical Research Institute, Seattle, WA 98121.
EMBO journal (ENGLAND) Dec 1992, 11 (12) p4313-21, ISSN 0261-4189 Journal Code: EMB
Contract/Grant No.: AI26296, AI, NIAID; GM43257, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Signals delivered to B cells via CD40 can synergize with those provided by other B cell surface receptors to induce B cell proliferation and antibody class switching as well as modulate cytokine production and cell adhesion. Recently, it has been shown that the ligand for CD40 is a cell surface protein of approximately 39 kDa expressed by activated T cells, gp39. Here we report on the isolation and characterization of a **cDNA** clone encoding human gp39, a type II membrane protein with homology to TNF, and the construction and characterization of a soluble recombinant form of gp39. COS cell transfectants expressing gp39 synergized with either anti-CD20 mAb or PMA to drive strong B cell proliferation and alone were able to drive B cells to proliferate weakly. In all cases the B cell proliferation induced by gp39-expressing COS cells was reduced to background levels by the addition of **soluble CD40** . Unlike gp39-expressing COS cells, recombinant soluble gp39 was not mitogenic alone and required co-stimulation to drive B cell proliferation. These results suggest that B cells require a second signal besides gp39-CD40 to drive proliferation and that soluble gp39 alone in a non-membrane bound form is able to provide co-stimulatory signals to B cells.

355738 99446899 PMID: 10519410
Potent activity of soluble **B7 -IgG fusion proteins in therapy of established** tumors **and as vaccine adjuvant.**
Sturmhoefel K; Lee K; Gray GS; Thomas J; Zollner R; O'Toole M; Swiniarski H; Dorner A; Wolf SF
Genetics Institute, Andover, Massachusetts 01810, USA. Knut.Sturmhoefel@emindustries.com
Cancer research (UNITED STATES) Oct 1 1999, 59 (19) p4964-72, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Fusion proteins consisting of the extracellular region of murine **B7** .1 or **B7** .2 and the Fc portion of murine IgG2a (**B7** -IgG) were evaluated for their ability to promote antitumor responses. Therapeutic administration of **soluble B7** -IgG in mice with established **tumors** induced complete regression of the **tumor** and increased the survival of mice. In three models, MethA, P815, and MB49, mice with 7-day-old established **tumors** were cured with two to three treatment cycles of **B7** -IgG, given twice a week. Even in mice with an established B16/F10 **tumor** (a poorly immunogenic melanoma), therapeutic treatment with **B7** -IgG alone slowed **tumor** growth and increased survival significantly. Still stronger antitumor activity was achieved when **B7** -IgG was used as a vaccine adjuvant mixed with irradiated **tumor** cells. In 80% of mice with 7-day-old B16 **tumors** , **tumors** regressed completely, and mice survived for at least 80 days. In all **tumor** models, **B7** .1-IgG and **B7** .2-IgG had similar antitumor activity. **B7** -IgG-mediated **tumor** rejection was dependent on T cells, specifically CD8 cells, as demonstrated by the failure of **B7** -IgG to induce **tumor** regression in severe combined immunodeficient or CD8-depleted mice. In addition, mice that were cured of an established **tumor** were protected against a rechallenge with the same **tumor** for at least 4 months, suggesting the generation of memory responses.

Surprisingly, the antitumor activity of **B7** -IgG was independent of IFN-gamma, as demonstrated by **tumor** rejection in IFN-gamma knockout mice. Our findings demonstrate the potent capacity of **B7** -IgG to generate or enhance antitumor immune responses and suggest the clinical value of **B7** -IgG.

Induction of therapeutic T-cell immunity by tumor **targeting with soluble recombinant** B7 **-immunoglobulin costimulatory molecules.**
Moro M; Gasparri AM; Pagano S; Bellone M; Tornaghi P; Veglia F; Corti A; Casorati G; Dellabona P
Immunochemistry Unit, and Cancer Immunotherapy and Gene Therapy Program, H. San Raffaele Scientific Institute, Milan, Italy.
Cancer research (UNITED STATES) Jun 1 1999, 59 (11) p2650-6, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Tumor targeting with immunomodulatory molecules is an attractive strategy to enhance the host's antitumor response. Expression of CD80 (**B7** -1) and CD86 (**B7** -2) costimulatory molecules in **tumor** cells has proven to be an efficient way to enhance their immunogenicity. Here, we studied the effects of **tumor** targeting with biotinylated recombinant **soluble** **B7** -1- and **B7** -2 immunoglobulin G molecules (bio- **B7** -IgG) using a pretargeting approach based on the sequential use of a biotinylated antitumor monoclonal antibody and avidin. Mouse RMA T-lymphoma cells bearing either bio- **B7** -1-IgG or bio- **B7** -2-IgG on their surface prime in vitro naive CD8+ CTLs, which are highly effective in adoptive immunotherapy, and induce therapeutic immunity when injected in **tumor** -bearing animals. In vivo targeting of established RMA **tumors** with bio- **B7** -IgG either cures **tumor** -bearing mice or significantly prolongs their survival. The antitumor response induced by targeted bio- **B7** -IgG depends on both CD4+ and CD8+ T cells. Moreover, **tumor** targeting with bio- **B7** -IgG in vivo is critical for both expansion in lymphoid organs and mobilization into the **tumor** of **tumor** -specific CD8+ CTLs. When targeting is performed on poorly immunogenic TS/A mammary adenocarcinoma, only bio- **B7** -1-IgG primes naive CTLs in vitro and cures or significantly prolongs the survival of **tumor** -bearing mice in vivo, confirming that the two costimulatory molecules are not redundant with this **tumor** . Altogether, these data suggest that **tumor** avidination and targeting with soluble bio- **B7** -IgG may represent a promising strategy to enhance the antitumor response in the host.
08143055 Genuine Article#: 251GE Number of References: 0
Title: Soluble B7 **-IgG as vaccine adjuvant for therapy of** cancer
Author(s): Sturmhoefel K; Lee K; Gray GS; Zollner R; Thomas J; Wolf SF
Corporate Source: GENET INST INC,/CAMBRIDGE//MA/02140
Journal: EUROPEAN JOURNAL OF CANCER, 1999, V35, 5 (OCT), PS10-S10
ISSN: 0959-8049 Publication date: 19991000
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND
Language: English Document Type: MEETING ABSTRACT

10/3,AB/10 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11876379 BIOSIS NO.: 199900122488
Systemic treatment with soluble B7 **-IgG fusion proteins significantly prolongs the survival of leukemic mice.**
AUTHOR: Dunussi-Joannopoulos K; Runyon K; Sturmhoefel K; Schaub R G; Leonard J P
AUTHOR ADDRESS: Genet. Inst. Inc., Andover, MA**USA
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p617A Nov. 15, 1998
CONFERENCE/MEETING: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998
SPONSOR: The American Society of Heamatology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

Surprisingly, the antitumor activity of **B7** -IgG was independent of IFN-gamma, as demonstrated by **tumor** rejection in IFN-gamma knockout mice. Our findings demonstrate the potent capacity of **B7** -IgG to generate or enhance antitumor immune responses and suggest the clinical value of **B7** -IgG.

Induction of therapeutic T-cell immunity by tumor **targeting with soluble recombinant** B7 **-immunoglobulin costimulatory molecules.**
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Journal: EUROPEAN JOURNAL OF CANCER, 1999, V35, 5 (OCT), PS10-S10
ISSN: 0959-8049 Publication date: 19991000
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND
Language: English Document Type: MEETING ABSTRACT

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AUTHOR: Dunussi-Joannopoulos K; Runyon K; Sturmhoefel K; Schaub R G; Leonard J P
AUTHOR ADDRESS: Genet. Inst. Inc., Andover, MA**USA
JOURNAL: Blood 92 (10 SUPPL. 1 PART 1-2):p617A Nov. 15, 1998
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ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English